DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/06/08 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transdermal patch comprising granisetron, does not reasonably provide enablement for a method for the treatment and/or prophylaxis of a patient having, or susceptible to, a condition selected from the group consisting of: pruritus, fibromyalgia and pain associated therewith, migraine, anxiety, cognitive and psychotic disorders, depression, schizophrenia, psychosis in postnatal depression, irritable bowel syndrome, alcoholism, obstructive sleep disturbed breathing, motion sickness, loss of cognitive function, urinary incontinence, dyskinesia, systemic lupus erythematosus, drug-induced pruritus, premature ejaculation, eating disorders,

obsessive compulsive disorder, gastric motility disorders, chronic fatigue syndrome, dyspepsia and cocaine dependence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: 1) breadth of the claims; 2) nature of the invention; 3) state of the prior art; 4) amount of direction provided by the inventor; 5) the level of predictability in the art; 6) the existence of working examples; 7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and 8)relative skill in the art. All of the factors have been considered with regard to the claims, with the most relevant factors being discussed below:

Breadth of the claims is broad. Claim 32 is directed to a transdermal patch comprising granisetron suitable for the treatment or prophylaxis of about 26 different conditions.

Amount of direction provided by the inventor, and quantity of experimentation needed to use the invention: while the present specification disclosed that the patch of the present invention are suitable for the treatment of any form of nausea and emesis associated with activation of 5-HT_3 receptors, such as with cancer therapy (page 9, 4th paragraph), the specification fails to describe how to precisely achieve the claimed method for the treatment and/or prophylaxis of a patient having multitudes condition such as: pruritus, fibromyalgia and pain associated therewith, migraine, anxiety, cognitive and psychotic disorders, depression,

schizophrenia, psychosis in postnatal depression, irritable bowel syndrome, alcoholism, obstructive sleep disturbed breathing, motion sickness, loss of cognitive function, urinary incontinence, dyskinesia, systemic lupus erythematosus, drug-induced pruritus, premature ejaculation, eating disorders, obsessive compulsive disorder, gastric motility disorders, chronic fatigue syndrome, dyspepsia and cocaine dependence. Let alone the patch recited in claim 1 without any specific amount of active agent.

There is no evidence from the present specification showing that applying a granisetron patch of the present invention can treat patient with condition such as schizophrenia, alcoholism, chronic fatigue syndrome, or depression. There is no evidence of correlation between these conditions, much less, 26 different conditions using one same patch of granisetron. Consequently, a burdensome amount of research would be required by one of ordinary skill in the art to use the claimed transdermal patch without undue experimentation.

As such, the practitioner would turn to trial and error experimentation in order to compose the claimed composition for the treatment of condition such as: pruritus, fibromyalgia and pain associated therewith, migraine, anxiety, cognitive and psychotic disorders, depression, schizophrenia, psychosis in postnatal depression, irritable bowel syndrome, alcoholism, obstructive sleep disturbed breathing, motion sickness, loss of cognitive function, urinary incontinence, dyskinesia, systemic lupus erythematosus, drug-induced pruritus, premature ejaculation, eating disorders, obsessive compulsive disorder, gastric motility disorders, chronic fatigue syndrome, dyspepsia and cocaine dependence, without guidance from the specification or the prior art.

The relative skill of those in the art: the skill of one of ordinary skill in the art is very high, e.g., Ph.D. and M.D. level technology.

Claims 1-26 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. While page 17 of the present specification shows the stability test for the claimed granisetron patch at 25°C and 40°C at 6 weeks storage period, the specification however, does not appear to provide support for the limitation "at least 6 weeks" a recited in the claims. The phrase "at least" suggests limitation beyond 6 weeks that includes 7, 8, 9 weeks or months or years. Further, the present specification does not appear to provide support for the limitation "0.5 to 20% w/w of a monomer containing a non-acidic hydroxyl moieties", recited in line 6 of claim 1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 and 28-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "a physiologically effective amount of granisetron loaded in the adhesive" in line 7. It is not entirely clear if the granisetron is loaded in the "acrylic adhesive" composition in line 4, or the granisetron is loaded in the adhesive patch.

Claim Rejections - 35 USC § 103

Claims 1-26, 28-31, 33 and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Effing et al. WO 98/53815 A1, in view of Miranda et al. US 5,656,286 or Horn et al. US 3,269,994.

Effing teaches a transdermal drug delivery device or a pressure sensitive skin adhesive device comprising an adhesive layer containing: 1) a copolymer of one or more A monomers and one or more B monomers, and 2) a therapeutically effective amount of granisetron as an active agent (abstract; page 2, lines 14-28; and claims 1 & 11). A monomers include n-butyl, and 2-ethylhexyl acrylates or methacrylates (page 4, 2nd paragraph; and claim 10). Active agent presents in the device ranges from 4-15% (page 5, lines 28-29). Effing further teaches the device has a surface area of about 15 cm^2 to about 60 cm^2 (page 7, lines 20-22). The device comprising granisetron is useful for the treatment of emesis and/or nausea during chemotherapy (abstract; page 1, lines 23-27; page 3, lines 1-5; and page 7, lines 23-29). The device shows stability at storage conditions under 25°C and 40°C after 4 weeks (examples 1 & 2).

Effing does not expressly teach the claimed transdermal patch with specific amounts of monomers.

Miranda teaches a transdermal composition comprising an adhesive layer comprising from about 2% to about 95% polyacrylate polymer (abstract; column 7, lines 20-29; column 9, lines 34-59; and column 10, lines 37-45). Polyacrylate polymer comprising at least 50% by weight of an acrylate or alkyl acrylate monomer, and from 0-20% of a functional monomer copolymerizable with the acrylate (column 10, lines 46-57). Acrylate monomer includes butyl acrylate or 2-ethylhexyl acrylate. Functional monomer includes acrylic acid or methacrylic acid such as hydroxyethyl meth(acrylate), and hydroxypropyl meth(acrylate) (column 10, lines 58 through column 11, lines 1-7). The adhesive layer further comprises from about 0.1% to about 50% drug including an antinauseant agent such as granisetron (column 10, lines 13-20; column 22, lines 38-42; and claim 62).

Horn teaches an adhesive coating comprising from about 70% to about 97% Group I monomer, and from about 30% to about 3% Group II monomer (column 2, lines 67 through column 3, lines 1-3). Group I monomer includes butyl acrylate or 2-ethylhexyl acrylate (column 2, lines 32-39). Group II monomer includes hydroxymethyl acrylate, hydroxyethyl acrylate, hydroxypropyl acrylate, and corresponding esters of methacrylic acid in place of the acrylic acid esters thereof (column 2, lines 57-65).

Thus, it would have been obvious to one of ordinary skill in the art to optimize the transdermal composition of Effing in view of the teachings of Miranda or Horn to obtain the claimed invention. This is because Miranda teaches a transdermal composition that can prevent crystallization of the drug (stability) without effecting the rate of drug delivery from the composition, because Miranda teaches a transdermal composition

suitable for a wide variety of drugs including granisetron, because Horn teaches a storage stable adhesive patch useful for a wide variety of purples (column 1, lines 17-68), and because Effing teaches the desirability for obtaining a stable transdermal composition suitable for granisetron.

It is noted that the cited references do not teach the claimed properties, such as the release profiles, as well as the storage stability. However, the burden is shifted to applicant to show that the adhesive compositions taught by Miranda or Horn do not exhibit the claimed properties, because Miranda teaches the same transdermal composition using the same acrylic adhesive and in the claimed amount.

Claims 1-26 and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seo et al. WO 00/47208 A1, in view of Miranda et al. US 5,656,286 or Horn et al. US 3,269,994.

Seo teaches a transdermal composition comprising an anti-vomiting agent such as granisetron (abstract; and pages 5-6).

It is noted that Seo does not expressly teach the claimed transdermal patch with specific amounts of monomers.

Miranda teaches a transdermal composition comprising an adhesive layer comprising from about 2% to about 95% polyacrylate polymer (abstract; column 7, lines 20-29; column 9, lines 34-59; and column 10, lines 37-45). Polyacrylate polymer comprising at least 50% by weight of an acrylate or alkyl acrylate monomer, and from 0-20% of a functional monomer copolymerizable with the acrylate (column 10, lines 46-

57). Acrylate monomer includes butyl acrylate or 2-ethylhexyl acrylate. Functional monomer includes acrylic acid or methacrylic acid such as hydroxyethyl meth(acrylate), and hydroxypropyl meth(acrylate) (column 10, lines 58 through column 11, lines 1-7). The adhesive layer further comprises from about 0.1% to about 50% drug including an antinauseant agent such as granisetron (column 10, lines 13-20; column 22, lines 38-42; and claim 62).

Horn teaches an adhesive coating comprising from about 70% to about 97% Group I monomer, and from about 30% to about 3% Group II monomer (column 2, lines 67 through column 3, lines 1-3). Group I monomer includes butyl acrylate or 2-ethylhexyl acrylate (column 2, lines 32-39). Group II monomer includes hydroxymethyl acrylate, hydroxyethyl acrylate, hydroxypropyl acrylate, and corresponding esters of methacrylic acid in place of the acrylic acid esters thereof (column 2, lines 57-65).

Thus, it would have been obvious to one of ordinary skill in the art to optimize the transdermal composition of Seo in view of the teachings of Miranda or Horn to obtain the claimed invention. This is because Miranda teaches a transdermal composition that can prevent crystallization of the drug (increases flux, and prevents skin irritation) without effecting the rate of drug delivery from the composition (abstract; and column 2, lines 19-23), because Miranda teaches a transdermal composition suitable for a wide variety of drugs including granisetron, because Horn teaches a storage stable adhesive patch useful for a wide variety of purples (column 1, lines 17-68), and because Seo teaches the desirability for obtaining a transdermal composition suitable for delivering granisetron over a period of day or more without skin irritation.

It is noted that the cited references do not teach the claimed properties, such as the release profiles, as well as the storage stability. However, the burden is shifted to applicant to show that the adhesive compositions taught by Miranda or Horn do not exhibit the claimed properties, because Miranda teaches the same transdermal composition using the same acrylic adhesive and in the claimed amount.

Response to Arguments

Applicant's arguments filed 11/06/08 have been fully considered but they are not persuasive.

Applicant argues that Effing Example 7 is the only example that employs an adhesive having a nucleophilic group, and is shown to lose 10% of its tropisetron content after just 4 weeks storage at room temperature. It is of note that the adhesive employed in Effing example 7 is the only adhesive employed by Effing that causes reduction in tropisetron content of the result patch, tropisetron being stable in all of the other adhesives tested.

However, in response to applicant's argument, it is note that in example 7, Effing uses a different adhesive composition. Further, Miranda and Horn are cited for the teachings of applicant's claimed adhesive composition, which comprise the claimed monomers and in the claimed amounts.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615